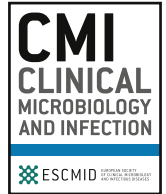




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## Letter to the Editor

## Does SARS-CoV-2 re-infection depend on virus variant?

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## To the Editor,

Knowledge about the degree of protection against re-infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is limited. A large observational study conducted among more than 500 000 people, in Denmark addressing infection rates during the last 4 months of 2020 showed that 0.7% of individuals who tested positive by PCR in early 2020 tested positive again in late 2020, and 3.3% of those who tested negative in early 2020, tested positive in late 2020. Protection rate against repeat infection was therefore 80.5% [1]. In Marseille, France—where large-scale SARS-CoV-2 PCR testing was proposed for the population from the beginning of the epidemic—we detected 47 165 cases of coronavirus disease 2019 (COVID-19) from February 2020 to mid-May 2021. The epidemic evolved in three successive waves (Fig. 1). The first wave was due to three major clades (20A, 20B and 20C strains) originating from Wuhan, China and was characterized by a bell-shaped epidemiological curve characteristic for seasonal respiratory infections and nearly disappeared around May 2020. The second wave took place between mid-June 2020 and February 2021 and was linked to the Marseille-1 variant (M1V), which had an African origin, and to the Marseille-4 variant (M4V), probably originating from a mink farm in the north of

France. M1V reached a very weak peak of incidence but accounted for up to 100% of infections during part of July 2020, then disappeared after 1.5 months [2], whereas incidence of the M4V that appeared in July 2020 showed an atypical wave shape and continued to account for a significant proportion of the cases in February 2021, indicating a duration of 7 months [3]. Finally, the third wave due to N501Y variant (N501YV), previously identified in the UK, South Africa and Brazil, started in early 2021, peaked in early April 2021 and numbers of cases are now rapidly decreasing. Fifty-eight cases of SARS-CoV-2 re-infection, as defined by two waves occurring at least 90 days apart, were observed during the second wave, representing 0.20% of the 29 154 COVID-19 cases observed during this wave. Of these 58 cases, 32 were primarily infected during the first wave, accounting for 0.11% of COVID-19 cases during the second wave and 26 were primarily infected during the second wave, accounting for 0.09% of COVID-19 cases during the second wave. Thirty-one cases of re-infection were observed during the third wave, accounting for 0.28% of the 11 262 cases diagnosed as of 18 May 2021. Of these 31 cases, nine were primarily infected during the first wave, accounting for 0.08% of COVID-19 cases during the third wave, 22 were primarily infected during the second wave, accounting for 0.19% of COVID-19 cases during the second wave and one was infected twice during the third wave.

Overall, re-infections accounted for 0.14% of cases diagnosed during the second and third waves of COVID-19 in Marseille. Of 6749 cases diagnosed during the first wave, 41 led to a re-infection (0.61%), whereas of 29 154 cases diagnosed during the second wave, 47 led to a re-infection (0.08%), which is significantly less ( $p < 0.001$ ;  $\chi^2$  test). This 0.61% re-infection rate is in line with the 0.7% rate in a Danish study in patients primarily infected in early 2020 [1]. We previously reported that M4V led to more severe infections than clade 20A and that N501YV infections were less severe than M4V infections [4]. We cannot exclude that patients could have been diagnosed outside our Institute; however, our

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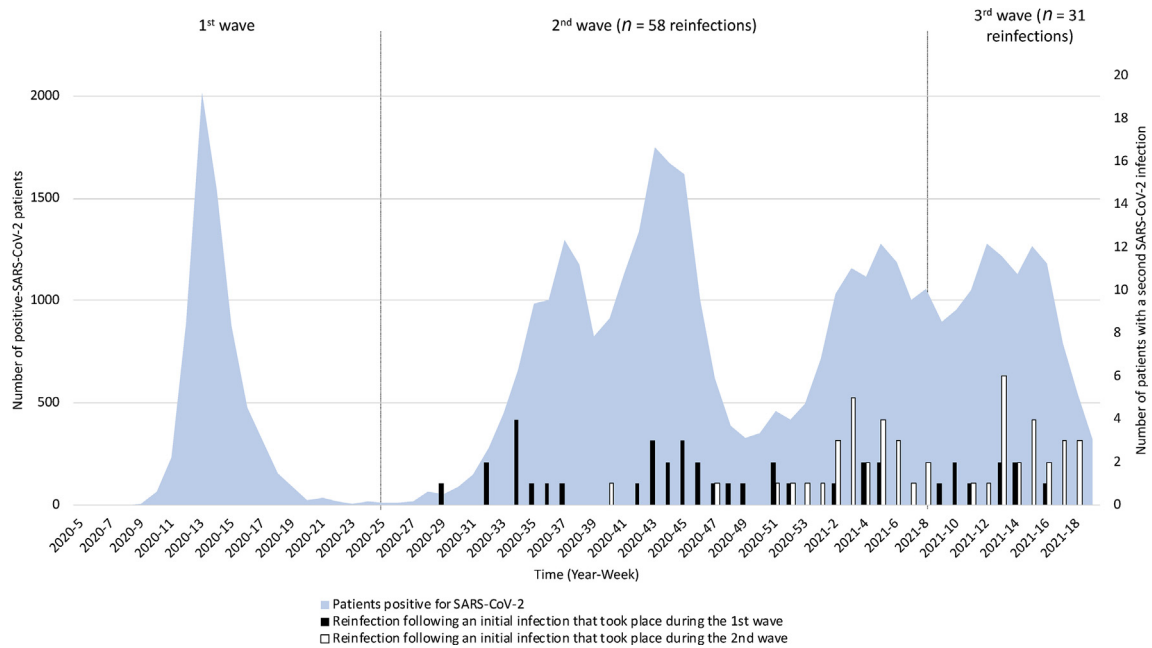


Fig. 1. Dynamic of SARS-CoV-2 infections and re-infections diagnosed at IHU Méditerranée Infection, 2020–2021.

Institute remained consistently the main laboratory performing SARS-CoV-2 PCR testing in the Marseille area from the start of the epidemic. Re-infections could also have been underestimated as some individuals with mild to moderate symptoms may not have been tested, especially in the second or third waves of the pandemic. Altogether, these data suggest that clades circulating during the first wave of COVID-19 in Marseille conferred less protection against re-infection than the variants mostly circulating during the second wave. This might be due to mutations in the SARS-CoV-2 spike protein affecting polyclonal antibody recognition leading to immune escape [5]. Further work including serological investigations would be of interest.

### Transparency declaration

DR has consulting fees: HITACHI Electronic Microscopy. The authors declare that they have no conflicts of interest.

### Author contributions

Conceptualization: Didier Raoult; Investigation: Linda Houhamdi, Nhu Ngoc Nguyen, Van Thuan Hoang; Formal analysis: Audrey Giraud-Gatineau; Writing original draft: Philippe Gautret; Writing, reviewing and editing: Didier Raoult.

### Ethical approval

Ethical approval was obtained from the Marseille Institutional Review Board and Ethics Committee (No. 2020-016-03).

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